

***In the Claims***

Please cancel claim 11 without prejudice to or disclaimer of the subject matter therein.

Please rewrite claim 2 as follows:

2. (Amended) An antibody having [specific] binding affinity that is specific only to the 20 kDa presenilin 2 C-terminal fragment (PS2-CTF) [according to claim 1].

***Remarks***

Reconsideration of this Application is respectfully requested.

Upon entry of the foregoing amendment, claims 1-10 and 12 are pending in the application, with claims 1, 2, 9 and 12 being the independent claims. Claim 11 is sought to be canceled without prejudice to or disclaimer of the subject matter therein. These changes are believed to introduce no new matter and their entry is respectfully requested.

Based on the above amendments and the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

***Explanation of Amendments***

Claim 2 has been amended for clarity. No new matter is believed to have been added by these amendments.

***Sequence Listing***

As requested by the Examiner, submitted herewith is another computer readable copy of the sequence listing, previously filed April 24, 1998. In accordance with 37 C.F.R. § 1.821(f),

the information recorded in computer readable form is identical to the written sequence listing filed April 24, 1998.

***Declaration and Objection to the Specification***

The Examiner stated that the Declaration filed July 9, 1998 is defective because the serial number of the provisional application stated in the oath should be 60/044,262 and not 06/044,262. Accordingly, submitted herewith is a new executed Declaration. The specification has been amended to correct the serial number.

***Objections to the Drawings***

Drawings that comply with 37 C.F.R. § 1.84 will be submitted upon indication from the Examiner that the captioned application is allowable. It is respectfully requested that the objections to the drawings be held in abeyance until such indication.

***Rejections Under 35 U.S.C. § 102***

Claims 2-3 were rejected under 35 U.S.C. § 102(a) as being anticipated by Vito, P. *et al.*, *J. Biol. Chem.* 271:31025-31028 (1996). Applicants respectfully traverse.

Vito *et al.*, at pages 31026-27, discuss two polyclonals specific for amino acids 341-377 and 438-448 of PS2. The polyclonals of Vito *et al.* can bind to any PS2 having amino acids 341-377 or 438-448, i.e., full length PS2, normal C-terminal fragment of PS2 (25 KD), and the PS2 C-terminal fragment of the captioned invention (20 KD), as well as ALG-3 (by the polyclonal specific for amino acids 438-448 of PS2). Therefore, the polyclonal of Vito *et al.* is not "[a]n antibody having binding affinity that is specific only to the 20 kDa presenilin 2 C-terminal

fragment (PS2-CTF)" as required in claim 2. For these reasons, claim 3, which is directed to a method of detecting 20 kDa PS2-CTF using the antibody of claim 2, is also novel over Vito *et al.* Hence, it is respectfully requested that the 35 U.S.C. § 102(a) rejection of claims 2 and 3 over Vito *et al.* be withdrawn.

***Rejections Under 35 U.S.C. § 103***

Claim 4 was rejected under 35 U.S.C. § 103(a) as being unpatentable over Vito *et al.* in view of Dalbow *et al.*, U.S. Patent No. 4,116,776. Applicants respectfully traverse.

The article by Vito *et al.* is discussed above. Dalbow *et al.* fail to teach an antibody having specific binding affinity to the 20 kDa PS2 C-terminal fragment. Therefore, Dalbow *et al.* fail to remedy the deficiency of Vito *et al.* Hence, the 35 U.S.C. § 103(a) rejection of claim 4 should be withdrawn.

Claim 5 was rejected under 35 U.S.C. § 103(a) as being unpatentable over Vito *et al.* in view of Janeway, C.A., Jr. *et al.*, Immunobiology, New York, Current Biology (1997). Applicants respectfully traverse.

The article Vito *et al.* is discussed above. Janeway fails to teach an antibody having specific binding affinity to the 20 kDa PS2 C-terminal fragment. Therefore, Janeway fails to remedy the deficiency of Vito *et al.* Accordingly, the 35 U.S.C. § 103(a) rejection of claim 5 should be withdrawn.

Claims 9 and 10 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Tanzi, R.E. *et al.*, *Neurobiol. Dis.* 3:159-168 (1996) in view of Miller, D.K. *et al.*, *Ann. New York Acad. Sci.* 696:133-148 (1993).

According to the Examiner, "Tanzi *et al.* teaches an increase in the accumulation of the PS2-CTF in the detergent-resistant cell fraction of cells with the PS2 mutation, PS2-N141I, a mutation associated with an increased incidence of familial Alzheimer's disease (FAD)." Tanzi *et al.* attribute this work to Kim *et al.*, *Neurobiol. Aging* 17:S1555 (July 24, 1996). *See*, Tanzi *et al.*, page 164, left column.

In accordance with M.P.E.P. § 715.01(c) (Rev. Feb. 2000), submitted herewith is a copy of a Declaration of Co-Inventors Under 37 C.F.R. § 1.132 ("132 Declaration"), executed by Drs. Rudolph Tanzi and Tae-Wan Kim, establishing that the work disclosed in Kim *et al.* is their own and that the other co-authors of Kim *et al.* were merely working under Drs. Tanzi and Kim's direction, providing technical assistance, or providing a reagent used in the experiments. A copy of Kim *et al.* is attached to the 132 Declaration. Thus, the 132 Declaration is sufficient to remove Tanzi *et al.* as a reference under 35 U.S.C. § 102(a), as the work described in Tanzi *et al.* is the inventors' own work and the other co-authors of Kim *et al.* are not co-inventors of the captioned application. Miller *et al.* fail to teach a PS2 20 kDa C-terminal fragment. Hence, it is respectfully requested that the 35 U.S.C. § 103(a) rejection of claims 9 and 10 be withdrawn.

### ***Conclusion***

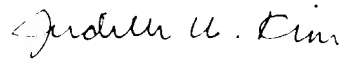
All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for

any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

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Attachment: A copy of Declaration of Co-Inventors Under 37 C.F.R. § 1.132, executed by  
Drs. Tanzi and Kim